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THE EFFECT OF RESTRAINING ON THE HEART RATE IN GUINEA PIGS

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Translation of "Vliv omebeni pohybu na sroeeni frekvenci morcat", Activitas Nervosa Superior, Vol. 10, No. 4, 1968, pp 382-388

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16. Abstract

The electrocardiography of laboratory animals is an electrophysiological technique becoming of interest to the pharmacologists and toxicologists for the following reasons: 1. It complements the neurophysical methods of obtaining data about the central nerve control of the vegetative functions; 2. It permits the study of the pharmacodynamic effect on excitable tissue whose cyclic changes of excitation can be often studied much easier than the changes in the central nerve functions.

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THE EFFECT OF RESTRAINING ON THE HEART RATE IN GUINEA PIGS

H. Mikiskova

The electrocardiography of laboratory animals is an electrophysiological technique becoming of interest to the pharmacologists and toxicologists for the following reasons:

1. First of all, it complements the neurophysical methods of obtaining data about the central nerve control of the vegetative functions;
2. It permits the study of the pharmacodynamic effect on excitable tissue whose cyclic changes of excitation can be often studied much easier than the changes in the central nerve functions.

The basic information about the heart rhythm, i.e., the point of origin of the heart excitation, rhythm regularity and mean heart frequency is often more important for the quantitative evaluation of the pharmacodynamic effects than other characteristics of the animal cardiograms. A detailed study of other characteristics often may help to analyze the mechanism of the effect of the materials (compounds) under study, however. (Mikisková and Mikiska, 1968).

During a regular activity the determination of the heart frequency is quite unambiguous and independent of the location of the electrodes, conductor system or technical parameters of the instrument used. In spite of that, the data in the literature pertaining to normal heart frequency for a certain animal species vary considerably. Often the differences in factors such as age and emotional state of the animal tested are not considered and these may be very important. We have systematically studied an effect of drugs on the cardiogram of a guinea pig as affected by these factors.

This work evaluates the emotional effect as related to different applications of electrodes and possibly fixation of the animal needed for a cardiographic examination. The study of electrocardiograms of guinea pigs in ontogenesis will be the subject of another communication.

A guinea pig is one of the most quiet laboratory animals and is, therefore, suitable for relatively easy ways to obtain long term

and reasonably undisturbed bioelectric potentials (ECG, EEG, EMG, etc.) in pharmacological and toxicological experiments. Many methods of the electrocardiographic registration still frequently used with animals affect their emotional state and are not suitable, considering the current development of the electrophysiologic techniques (e.g., application of needle electrodes). Some other methods, such as ECG in an unnatural fixation on the back, used by Bartmann and Reinert (1952) are justified only for special experiments, such as a thorough examination of all chest leads.

The use of light anesthesia (Lombard, 1952) or drastic restriction of the mobility of the animal (Pratt, 1938, Corwin et al, 1963) is necessary usually for a routine cardiography of smaller rodents, such as mice, hamsters, rats, but it is considered unnecessary for guinea pigs. The technique developed by Lukoschkova and Thiessen (1954) whereby the guinea pig is held in hand during registration may be suitable only for short term tests for orientation. A method due to Richtarik and Woolsley (1965) is more suitable for long term tests. The ECG is taken while the animal stands in a normal position on four electrodes located on the bottom of a box made from organic glass. The box restrict the mobility of the animal. The most adequate, however, is the way to take ECG on an animal which is unrestricted using radio telemetry or a flexible cable. Such methods are still rather rare and so far as we know, they have not been used for guinea pigs.

We took ECG on unrestricted guinea pigs in our laboratory using wire connections and radio telemetry and compared results obtained on animals tied to a fixation table.

METHODOLOGY

The ECG of guinea pigs was registered by an electroencephalograph (WTBG, Berlin) for one minute, one hour apart. The animals (males) were all subject to 2 to 3 dry runs to get used to the test conditions. All data about the age, weight of the animals as well as the number

number and duration of the experiments are shown in pertinent tables and graphs.

The following methods of registration were used:

1. Animals tied to the fixation table with abdomen down, ECG was taken using electrodes connected by means of radiotechnic "crocodiles". The skin of the legs of the animals was defiled and covered by electrocardiographic paste (Mikiska and Mikosková, 1964).

2. Animals moving freely, the use of radiotelemetry. To measure the potential, the electrodes used were in the form of a silver plate 8mm diameter, located in a body cut from organic glass (Figure 1). The electrodes were attached to the skin by means of colodium. The conductivity is achieved by a layer of paste, the wiring is connected by a nut. The electrodes were modified according to a larger type used for ECG of people during work (Vodolarskiy et al, 1961, Mikiska, 1967). The best location of electrodes on freely moving guinea pigs was on the vertex and the small of the back. This way the shape of ECG does not differ from a VF and the effect of electromyographic potential is present only when the movements of the animal are substantial. The test is performed in a quiet room and the animal remains in its own cage (without the top). The electrodes are connected to a transmitter, fixed to the back of the guinea pig by means of leather loops attached to the upper extremity and an elastic rubberband located under the abdomen. The transmitter is a scaled down version of that used for a telemetric ECG on humans (Mikiska, 1967, Mikiska and Hyška, 1967); the main difference being smaller capacity electrolytic condensators and lower voltage sources. The total mass of the transmitter was thus reduced to 70g. The schematics of the telemetric system, including both transmitter and receiver, is included in our complete report (Mikisková and Mikiska, 1968).

3. Animals moving freely, the use of connection by a flexible cable. The experiments were carried out in the same environment and with the same electrodes as the telemetric experiments described above. The electrodes, however, were connected to the instrument

directly with a two-line cable about 1 meter long. The results of the experiments with different methods are in Graph 1 and Table 1. In the case of fixed animals, the heart frequency remains remarkably stable; during six hours the drop in the heart frequency for the younger age group is on the average 1.9%. In the case of younger animals moving freely, the heart frequency slows down gradually, especially when the cable connection is used, the reduction is up to 29.2%. The changes in the older group are similar; however, the difference between the final and initial values in the case of freely moving animals is lower (on the average 21.2%).

Initial values of heart frequency in all experimental situations are lower for the older animals. When the animals move freely and connection is done by the cable, the frequencies for both age groups come close during the 5th and 6th hour.

The behavior of the older age group of guinea pigs is shown in Graph 2. On the right side of the graph, results from 17 experiments with 6 animals moving freely for 4 hours and fixed to a table for subsequent 2 hours are plotted. ECG was registered by means of a flexible cable. The heart frequency, reduced in average by 18% at the end of the 4th hour, returns immediately after the fixation to the initial value and remains there until the end of the experiment.

In the Table 1 and Graphs 1-2, the values are only average for the individual age groups and experimental situations. We could not find any significant differences between individuals during the experiments even after three repetitions.

DISCUSSION

The initial values of heart frequency of fixed guinea pigs found in our experiments are quite close to those found in other works (e.g., Richtarik and Woolsley, 1965). The slow down in frequency experienced in freely moving animals is much more pronounced for guinea pigs connected with the instrument by the thin cable

than in the case of animals with telemetric transmitter. Possibly the effect of the instrument, its way of installation and its weight has to be considered. The use of an implanted transmitter may produce better results.

We obtained similar results with freely moving rabbits, and found considerable slow down in heart beats, sometimes down to 150 beats per minute. For fixed rabbits Haberland and Regoeczi (1963) report the minimum of 200 beats per minute, a value similar to that reported in other works.

The slow down in heart frequency of freely moving animals under minimum values determined by a usual method and reported in test books was demonstrated by Essler and Folk (1961, 1962) by a series of experiments with a dog and a cat isolated in a sound-proofed room for several days, using telemetry. The authors did not find a similar effect when experimenting with a rabbit. Our experiments summed up in the right part of Graph 2 show that the fixation of the guinea pig is the main factor which causes the relatively constant heart frequency when measuring it the usual way, i.e., with the animal tied down. The value obtained in this manner is quite reproducible and, therefore, it is suitable for the use in applied research in spite of the fact that it is not "basal".

During the measurement of ECG in freely moving guinea pigs, the heart rate decreases during the experiment but the change occurs continuously and regularly; one can depend on it while designing an experiment. As an example, we can give the experiments with telemetric ECG during the exposure to carbon disulphide vapors (Mikisková and Mikiska, 1968). In some experiments the slow down of the heart beat can be utilized, e.g., analeptics even at low dosage will likely prevent it.

A guinea pig, unlike the smaller laboratory rodents, does not have pronounced switch from an activity to a deep sleep (Nicholls, 1922, Schwarz and Bickford, 1957, Veselovský, 1964, and Mikiska,

1965). Very likely this can be related to our finding that during the measurement of the heart activity of guinea pigs over a period of several hours, no significant variations in frequency are observed. As an example of such a measurement are results in Graph 3. In this graph several individual measurements of heart frequency done telemetrically on free moving guinea pigs of the weight range 450 to 580 g are depicted. For comparison a time dependent telemetric data obtained on a mouse by Ko and Neuman (1967) are shown.

TABLE 1

6 Pokusná situace	1 Doba od začátku pokusu (hod.)							2 Relativní střední chyba průměru	3 Počet	
	0	1	2	3	4	5	6		4 pokusů	5 zvířat
7 Mladší morčata[1]										
8 upoutaná ke stolku	362	366	360	357	355	354	355	±1,1 %	18	6
9 volně pohyblivá (s vysílačem)	365	352	330	325	320	320		±2,6 %	7	7
10 volně pohyblivá (spojení kablíkem)	343	290	270	265	251	249	243	±2,0 %	18	5
11 Starší morčata[2]										
upoutaná ke stolku	323	321	316	309	309	311	304	±1,8 %	18	5
12 volně pohyblivá 13 (s vysílačem)	304	275	278	270	272	268	264	±2,3 %	18	8
14 volně pohyblivá (spojení kablíkem)	237	274	255	251	244	242	234	±2,2 %	18	5

15 [1] = věk 2–4 měsíce, váha 330–580 g, [2] = věk 12–18 měsíců, váha 800–1100 g.

Key: 1--Time from start of experiment (hrs); 2--Relative mean error; 3--Number; 4--Experiments; 5--Animals; 6--Experimental situation; 7--Younger guinea pigs (1); 8--Fixed to a table; 9--Freely moving (with a transmitter); 10--Freely moving (with a cable); 11--Older guinea pigs (2); 12--Fixed to a table; 13--Freely moving (with a transmitter); 14--Freely moving (with a cable); 15--Notes (1) Age 2-4 months, weight 330 to 580g; (2) Age 12-18 months, weight 800 to 1100 g

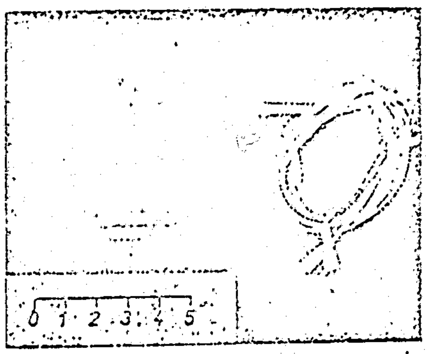
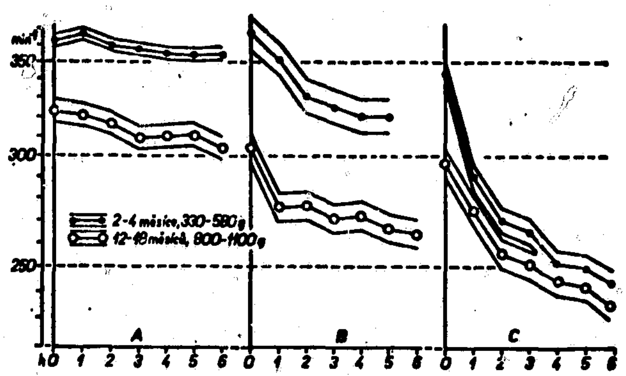


Figure 1. Transmitter and pick-up electrodes for the telemetric ECG of animals (scale in cm).



Graph 1: Average heart frequency of guinea pigs in three different situations:

A - Animals fixed to a table

B - Animals freely moving with a transmitter affixed to the back

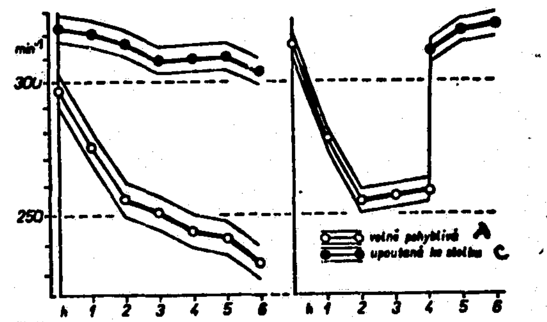
C - Animals freely moving connected to the instrument by a flexible cable

X--axis: Time from the start of the experiment

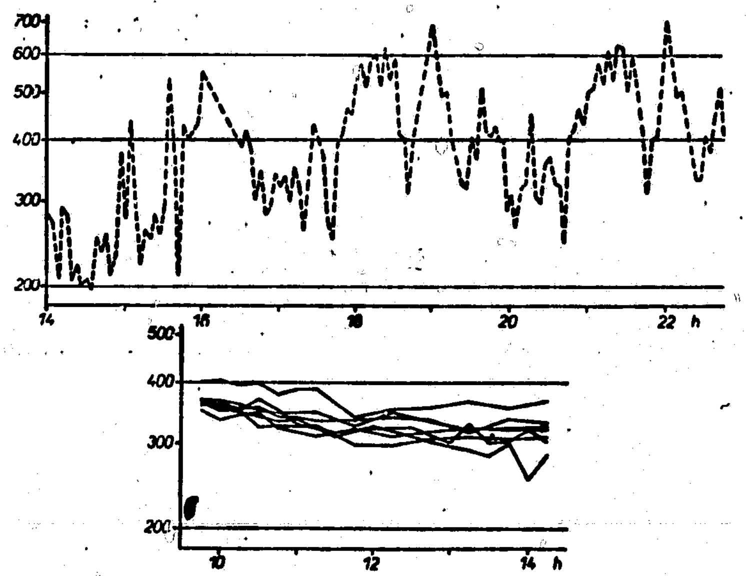
Y--axis: Heart frequency (in logarithmic scale)

circles - Average values of the heart frequency measured hourly

thin lines - Average ± mean error of average



Graph 2: <u>Right part</u> - Average heart frequency of guinea pigs (800 to 1100 g) freely moving for 4 hours, then fixed to a table for 2 hours;
<u>Left part</u> - 6-hour experiments for animals of the same age fixed (A) and freely moving (C). X and Y axis the same as in Graph 1.



Graph 3: Comparison of individually measured changes in telemetric ECG of guinea pigs (full line, our own results) and of mice (broken line, Ko and Neuman, 1967)

X--axis: The hour of the day

Y--axis: Heart frequency (in the logarithmic scale)

References

Bartman, K., Reinert, H. Extremity and Breast Wall EKG of a non-anethtisized Guinea Pig, Naunyn-Schmiedeberg's Arch. exp. Path. Pharmak., 1952, 216:258-267.

Corwin, A. H., Dukes-Dobos, F. N., Hamberger, M.: Bio-assay of Food Allergens. II. Food-induced Reactions of the Heart Rate of Guinea Pigs, Ann. Allergy, 1964, 21:547-562.

Essler, W. O.,Folk, G.E. Jr.: Determination of Physiological Rhythms of Unrestrained Animals by Radio Telemetry. Nature (Lond.), 190, 1961, 4770: 90-91.

Essler, W. O. Folk, G. E.Jr.: A Method of Determining True Resting Heart Rate of Unrestrained Mammals by Radio Telemetry. Anim. Behav., 10, 1952, 1-2: 168-170.

Haberland, G., Regoeczi, E.: The Constant Nature of the Heart Function of a Rabbit. Investigations using Synchronously Recorded Heart Current and Heart Sound Curves, Z. ges. exp. Med., 1963, 137: 123-143.

Ko, W. H. Neuman, M. R.: Implant Biotelemetry and Microelectronics. Science, 1967, 156: 351-360.

Lombard, E. A.: Electrocardiograms of Small Mammals, Amer. J. Physiol., 1952, 171: 189-193.

Lukoschek, P., Thiesen, J.: Normal Guinea Pig EKG Z. Kreisl.-forsch. 43, 1954: 172-180.

Mikiska, A.: Analysis of some Electrophysiological Methods with regard to their Utiliz ation in the Industrial Toxicology (Dissertation UHPChP* Prague, 1965.

Mikiska, A.: Short-distance Radio Telemetry of Biopotentials in Occupational Medicine. Z. Prav.-Med. 12, 1967: 48-62.

Mikiska, A. Radiotelemetry of Bioelectric Potentials in the Physiology of Labor, Pracov. Lek., 19, 1967: 211-223.

Mikiska, A., Mikiskova, H.: Determining Neurotoxicity by some Electrographic Methods (EEG, EKG, EMG) in Guinea Pigs. Activ. nerv. super. (Prague), 6, 1964: 56-59.

Mikiskova, H., Mikiska, A.: Some Electrophysiological Methods for Studying the Action of Narcotic Agents in Animals, with Special Reference to Industrial Solvents: A Review. Brit. J. Industr. Med., 25, 1968: 81-105.

Nicholls, E. E.: A Study of the Spontaneous Activity of the Guinea Pig. J. Comp. Pschol., 2, 1922: 303-330.

Pratt, C. L. G.: The Electrocardiogram of the Guinea Pig. J. Physiol. (Lond.), 92, 1938: 268-272.

Richtarik, A., Woolsey, T. A., Valdivia, E.: Methods for Recording ECG's in Unanesthetized Guinea Pigs. J. appl. Physiol. 20, 1965: 1091-1093.

Schwarz, B. E., Bickford, R.: Electroencephalographic Changes in Animals under the Influence of Hypnosis. J. nerv. ment. Dis. 124, 1957: 433.

Vesolovsky, Z.: The Most Common Animals, Prague, Mlada fronta, 1964.

Vodolazsky, L. A., Podoba, E. V., Solovyeva, V. P.: Further Development of the Method of Recording of Electrocardiograms and Electromyograms of a Worker during his Work in the Factory. Digest Internat. Conf. Med. Electronics, New York City, 1961.

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